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09/697,297	10/27/2000	James M. Robl	P 0277165	3475

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EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/697,297	Robl et al.
Examiner	**Art Unit**
Joseph Woitach	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 21, 2002*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1 and 3-57* is/are pending in the application.

4a) Of the above, claim(s) *17-32, 36-38, 48, and 55-57* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3-16, 33-35, 39-47, and 49-54* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Oct 27, 2000* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This application, filed October 27, 2000, claims benefit to provisional application 60/161,987, filed October 28, 1999.

Applicants' amendment filed November 21, 2002, paper number 9, has been received and entered. The specification has been amended. Claim 2 has been canceled. Claims 1, 3-5, 9-11, 13 and 14 have been amended. Claims 39-57 have been added. Claims 1, 3-57 are pending.

Election/Restriction

As indicated in the previous office action groups I and II, claims 1-16, 33, 34 and 35 were rejoined and examined together. Claims 17-32 and 36-38 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 7.

Newly added claims 55-57 are drawn to a differentiated cell and would properly be restricted to group VI (see restriction requirement, page 3, paper number 5). Claim 48 is drawn to a method of differentiating the pluripotent embryonic stem cell and would be properly restricted to group VII (see restriction requirement, page 3, paper number 5).

In addition, the restriction requirement indicated that elected invention was drawn to a method for producing pluripotent embryonic stem cells wherein a haploid cell in metaphase II is used. Methods of use of the pluripotent embryonic stem cell, claims 13-16, were included in the

elected group. Claims 13, 14 have been amended to include providing 'differentiated cells' for implantation. Claims 13, 14 encompass the elected invention because they still include the limitation of providing pluripotent embryonic stem cells. However, newly amended claims 13, 14 are directed to an invention that is independent and distinct from the invention originally claimed for the following reasons: pluripotent embryonic stem cells and differentiated cells are materially different types of cells. The making and/or using of differentiated cells represents unique and distinct invention over the elected invention of making and using pluripotent embryonic stem cells.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1, 3-57 are pending. Claims 17-32, 36-38, 48, 55-57 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 7. Claims 1, 3-16, 33-35, 39-47, 49-54 are currently under examination as they are drawn to a method for producing pluripotent embryonic stem cells wherein a haploid cell in metaphase II is used and methods of use of said pluripotent embryonic stem cells.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently

named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

The disclosure is objected to because the Brief Description of the Drawings contains references to labels which are not present in the figures is withdrawn.

The amendment to the specification deleting the unclear references has obviated the basis of the objection.

Priority

Applicant has complied with the conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) by amending the first line in specification to benefit to provisional application 60/161,987, filed October 18, 1999. It is noted that the executed declaration , paper number 3, contains reference to the provisional application.

Claim Objections

Claims 13, 14, 39, 40, 49 and 50 are objected to because of the following informalities: As discussed above and as set forth in the restriction requirement the elected invention is drawn to a method for producing pluripotent embryonic stem cells wherein a haploid cell in metaphase

II is used. Claims 13, 14, 49 and 50 recite use of 'differentiated cells' which are not encompassed by the elected invention of pluripotent embryonic stem cells. Claim 39 recites a first step of providing an embryo which is broader than using a haploid cell in metaphase II and encompasses inventions of groups III and IV, and other methodologies not specifically set forth in the claims or specification. Claim 40 recites transferring a haploid cell or nucleus into an enucleated blastomere which is also broader than using a haploid cell in metaphase II. Claims 13, 14, 39, 40, 49 and 50 should be amended to reflect the elected invention.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-9, 11-16 and 33-35 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of using a haploid secondary oocyte with one polar body, does not reasonably provide enablement for use of haploid male germ cells is withdrawn.

The amendment to the claims to encompass 'obtaining an oocyte in metaphase II' has obviated the basis of the rejection. As set forth in the previous rejection the specification

provides no guidance or teaching on how to affect the presently claimed methods in male germ cells or in blastomere. The claims now encompass the use of an oocyte which the specification provides art recognized methods for activating and culturing. With respect to newly added claims, the claims encompass 'preparing an embryo' and would not be subject to the basis of the previous rejection.

Claims 1, 3-16, 33-35, 39-47, 49-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Specifically, claim 1 recites '(a) obtaining an oocyte in metaphase II that comprises DNA derived from a single individual male or female mammal' and then specific method steps for activating the oocyte, however the specification does not support the combination of these method steps. A review of the specification indicates obtaining an oocyte in metaphase II and performing steps (b)-(d) are contemplated (page 18, lines 16-30). Further, support is found for providing an enucleated cell/oocyte and transplanting into said enucleated oocyte two male or female haploid nuclei, e.g. derived from oocyte or sperm, and activation by an appropriate activation procedure (page 19, lines 1-8), however there is no support for using the methods of

preventing the second polar body extrusion with a diploid nuclear transfer unit produced by this method. The specification only provides methods of producing a diploid oocyte/embryo either by (1) preventing the polar body loss or by (2) providing a diploid nuclear transfer unit. In light of the teachings of the specification, practicing the methods as claimed would result in an activated oocyte with a diploid genome derived from a male or female mammal and a third haploid complement of the genome provided by the polar body. The specification provides methods to produce embryonic stem cells however practicing the method as instantly claimed does not have literal or figurative support in the instant disclosure. Further, the methods as instantly set forth would result in a cell which has three copies of chromosomes, and the specification is silent to culture conditions which would be necessary to culture the resulting triploid cell into an embryo in order to isolate the ICM or stem cells. Similarly, claim 39, as more specifically set forth in claim 40, encompasses transferring a haploid cell or haploid nucleus, however the specification only provides the specific support for transplanting two haploid nuclei and activation of the resulting nuclear transfer unit. The specification does not support providing a single haploid nuclei to an enucleated blastomere and combining it only with the specific method step of inhibiting the first cleavage. Examiner has reviewed the portions of the specification indicated as supporting the new claims and claim amendments (see Applicants amendment, bridging pages 9-10), and it is noted that literal support for the terms recited in the claims are found at the passages indicated. However, as indicated above the portions of the

specification relied upon does not provide support for the combination of specific method steps recited in the present claims.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 1, 3-16, 33-35, 39-47, 49-54 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

As noted above, even if literal support for combining the embodiments would be found to be supported by the present specification, the instantly claimed method would result in a cell that is triploid. The triploid cell would not be viable or would not be capable of producing pluripotent embryonic stem cells. The specification is silent to conditions for culturing triploid cells into diploid cells or more generally into pluripotent embryonic stem cells. Further, having the DNA of the polar body in addition to the DNA derived form a single male or female would not make the resulting activated oocyte gynogenetic or androgenetic as required in claim 1. The dependent claims are included in the basis of the rejection because they recite specific embodiments which combinations were not specifically contemplated or enabled by the specification. In addition, newly added claims are drawn to the use of a blastomere, however a blastomere does not undergo metaphase II, and the specification is silent with respect to methods to induce a blastomere to undergo meiosis and precede through metaphase II. In view of the lack

of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-16 and 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

The amendments to the claims have obviated the basis of the rejections.

Newly added claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 42 recites the limitation "the blastomere", however there is insufficient antecedent basis for this limitation in the claim or in independent claim 39.

Newly added claims 52-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 52 recites and is drawn to the limitation "Pluripotent cells", however there is insufficient antecedent basis for this limitation in independent claim 39 because several of the cells produced during the method are pluripotent, the embryo, inner cell mass cells and cells derived therefrom. It is unclear to which pluripotential cell the claim 52 refers. Claims 53 and 54 do not further clarify the basis of the rejection and only point to the specific species source of the cell

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 33 and 34 stand rejected and newly added claims 52 and 53 are under 35U.S.C. 102(a/e) as being anticipated by Thomson (US Patent 5,843,780).

Applicants summarize the teachings of 5,843,780, noting that the method used to prepare the embryonic stem cells in '780 is different than that disclosed in the instant specification. It is noted that genome in the embryonic cells in '780 represents a genome that would be different from that of the cell instantly claimed. Further, Applicants state that the instantly claimed cells are phenotypically different from those disclosed in '780 because the embryonic stem cells in '780 are capable of giving rise to a complete organism, whereas the instantly claimed embryonic stem cells are not. Applicants argue that the pluripotent cells of the present invention are materially, structurally, and functionally different from those disclosed in the '780 patent. See Applicants' amendment, page 13. Applicants' arguments have been fully considered, but not found persuasive.

First, with respect to arguments that the cells are functionally and in part materially different in view of how the instantly claimed cell was generated, it is noted that the art teaches

that mammals can be cloned from DNA derived from a single individual. The cells resulting from nuclear transfer results in an embryo which is capable of giving rise to a complete organism. In the case of the instantly claimed cells, the source of the DNA is derived from a single individual and is comprised in an activated oocyte, and thus is analogous to a cell which was derived by nuclear transfer. The specification does not teach that the instantly claimed cells are not capable of giving rise to a complete organism, and in view of the art of nuclear transfer there is no reason that an oocyte with DNA derived from a single individual would not be capable of giving rise to a complete organism. Therefore, arguments that the cells are functionally different are not found persuasive.

With respect to arguments that the cells are structurally and in part materially different because the resulting embryonic stem cells contain the genome derived from a single individual are not persuasive because this difference does not provide a distinguishing characteristic to the cell. The similarities and differences among the gemone of cells from different sources are inherent properties of the cell and dependent from where they are obtained. For example an embryonic stem cell produced by nuclear transfer with DNA derived from a single individual, produced by the instantly claimed methods wherein the DNA is derived from a single individual, or produced through the use of an embryo which is the result of fertilization using the gametes of parents of the single individual of the preceding methods would be indistinguishable. Comparing the genome of any of the cells produced by these methods would indicate the genomes are the same. Thus, in this case the method used to generate a cell would not provide a distinguishing

feature to the resulting cell. Additionally, it should be noted that a single individual from which DNA can be derived represents a source of DNA which represents both maternal and paternal sources. Arguments that the resulting embryonic stem cell comprises DNA from only a single individual is not persuasive because the single individual represents a source of DNA which is derived from two individuals. More generally, inherent similarities and differences between the genomes of single individuals exist and may provide a unique identify characteristic to an individual cell one from the other, however because the general similarities and differences are inherent properties of cells it would not provide a distinguishing feature to the instantly claimed embryonic stem cell. The claims are not drawn to DNA derived from a single specific individual, rather the breadth of the claim encompasses the use of DNA from any individual, and thus broadly encompasses cells comprising any variation of possible DNA. Applicants arguments that the cells are structurally unrelated are not persuasive because the cells are a product by process and the process does not produce a cell which can be distinguished from a cell produced by other methods, and more generally because of the breadth of the claim, does not provide a material or structural characteristic which would distinguish the claimed cell from any other cell isolated or produced by other means.

As noted in the previous office action, the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the

burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989). In the instant case, Applicants arguments are not persuasive because the methods used to produce the instantly claimed cells produce cells which are materially, structurally and functionally the same as those disclosed by Thomson.

Like claims 33 and 34, newly added claims 52 and 53 encompass primate pluripotent embryonic stem cells produced by the method of claim 39. Though claim 39 recites different method steps, the claims are interpreted as they are directed to the elected invention. The cells of claims 52 and 53 are a product by process, and in view of the teaching in the present specification are representative of pluripotent stem cells obtained by other means, in particular those derived from the inner cell mass of a blastocyst. Thomson teaches methods of obtaining primate embryonic stem cells from the inner cell mass of a primate. Thomson characterizes the isolated cells and demonstrates that the cells are representative of pluripotent embryonic stem cells. Thus, the cells taught by Thomson anticipates the instantly claimed cells.

Claims 33-35 stand rejected and newly added claims 52-54 are rejected under 35 U.S.C. 102(e) as being anticipated by Thomson (US Patent 6,200,806).

Applicants note the teaching of 6,200,806 are substantially identical to 5,843,780 describing the isolation of human pluripotent embryonic stem cells. Applicants note that the

embryonic stem cells generated by Thomson are derived from embryos representing maternal and paternal sources of DNA, and as argued in traverse of the rejection made under 35 USC 102 over '780 the instantly claimed pluripotent embryonic stem cells of the present invention are materially, structurally, and functionally different from those disclosed in the '860 patent. See Applicants' amendment, page 14. Applicants' arguments have been fully considered, but not found persuasive.

As set forth above, with respect to arguments that the cells are functionally and in part materially different in view of how the instantly claimed cell was generated, arguments that the cells are functionally different are not found persuasive because the instant specification does not teach that the instantly claimed cells are not capable of giving rise to a complete organism, and in view of the art of nuclear transfer there is no reason that an oocyte with DNA derived from a single individual would not be capable of giving rise to a complete organism. With respect to arguments that the cells are structurally and in part materially different Applicants arguments are not persuasive because the cells are a product by process and the process does not produce a cell which can be distinguished from a cell produced by other methods, and more generally because of the breadth of the claim, does not provide a material or structural characteristic which would distinguish the claimed cell from any other cell isolated or produced by other means.

As noted above and in the previous office action, the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and

functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989). In the instant case, Applicants arguments are not persuasive because the methods used to produce the instantly claimed cells produce embryonic stem cell which are materially, structurally and functionally the same as those disclosed by Thomson.

Additionally, like claim 35, claim 54 encompasses human pluripotent embryonic stem cells produced by the method of claim 39. Thomson teaches methods of obtaining human embryonic stem cells from the inner cell mass of a blastocyst. Thomson characterizes the isolated cells and demonstrates that the cells are representative of pluripotent embryonic stem cells. Thus, the cells taught by Thomson anticipates the instantly claimed cells.

Claims 1, 3-9, 11-13 and 33 stand rejected and newly added claims 39, 43, 44, 46, 49 and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Newman-Smith *et al.* (Development, 1995).

Applicants note the requirements of the pending claims pointing in particular to step (d) which requires that the cells are cultured 'in an undifferentiated pluripotent state'. Applicants

summarize the teaching of Newman-Smith *et al.* and argue that the parthenote ICM taught by Newman-Smith *et al.* have a defect which leads to the differentiation of the stem cells into parietal endoderm cells. Applicants note that the present claims require culturing the resulting inner cell mass in an undifferentiated state and argue that Newman-Smith *et al.* fails to teach this limitation. See Applicants arguments, pages 15-16. Applicants' arguments have been fully considered, but not found persuasive.

First, the instant claims do not require that all the cells form the ICM to be maintained in an undifferentiated state or for any specific length of time. Examiner acknowledges that Newman-Smith *et al.* teach that there is a predisposition of the stem cells from the ICM of a parthenote to become parietal endoderm cells. However, Newman-Smith *et al.* teach that some stem cells are maintained in the ICM culture when tested. For example, Newman-Smith *et al.* could detect SSEA-1 positive cells in ICM cultures (page 2072, first paragraph), or positive for LN (page 2072, first full paragraph). Therefore, the methods taught by Newman-Smith *et al.* anticipate the claims as broadly set forth.

Second, it is noted that Newman-Smith *et al.* specifically recognized the propensity of ICM cells of parthenotes to preferentially differentiated into parietal endoderm cells and discuss specific culturing conditions to increase and maintain the number of ICM cell in the culture. For example, Newman-Smith *et al.* teach that addition of a polynucleotide encoding Igf-1r to a blastomere produced high expression of said protein and when treated with Igf-2 had 'significantly more ICM cells at the blastocyst stage' (page 2073, first full paragraph). Further,

Newman-Smith *et al.* teach that culturing the parthenote in ES/LIF medium with mouse SLN fibroblasts also increases the ICM population (page 2073, first full paragraph in second column). Applicants arguments are not persuasive because Newman-Smith *et al.* note the limitation discussed by Applicants and provide specific conditions for maintaining the ICM from a parthenote.

With respect to the other limitations encompassed by the claim, Newman-Smith *et al.* teach the isolation of inner cell mass cells from mouse embryos wherein parthenotes were generated by preventing the extrusion of the polar body by cytochalasisn D and then cultured to blastocyst stage of embryogenesis. The inner cell mass cells from the resulting embryo were isolated and cultured and analysis of the resulting cells indicated that some of the cells represented pluripotent stem cells. Finally, with respect to implanting the cells, Newman-Smith *et al.* also teach that similar experiments generating parthenotes indicated that embryos implanted into pseudo-pregnant females gave rise to embryos up to the appearance of limb buds (page 2069, second column).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made

> to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 11-16 and 33 stand rejected and newly added claims 39, 43, 44, 46-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Newman-Smith *et al.* (Development, 1995) in further view of Thomson ((US Patent 5,843,780).

Applicants argue as in traverse of the 35 USC 102 rejection over Newman-Smith *et al.*, Newman-Smith *et al.* fails to teach the instantly claimed method. Further, Applicants argue that the '780 patent only discloses cells derived from both a maternal and paternal parents, not a single individual. See Applicants amendment, pages 16-17. Applicants arguments have been fully considered, but not found persuasive.

As noted above, Newman-Smith *et al.* teach that there is a predisposition of the stem cells from the ICM of a parthenote to become parietal endoderm cells however, some stem cells are maintained in the ICM culture when tested. Therefore, the methods taught by Newman-Smith *et al.* anticipate the claims as broadly set forth. Further, Newman-Smith *et al.* specifically

recognized the propensity of ICM cells of parthenotes to preferentially differentiated into parietal endoderm cells and discuss specific culturing conditions to increase and maintain the number of ICM cell in the culture. Therefore, Applicants arguments are not persuasive because Newman-Smith *et al.* teach that ICM cells are observed when cultured and provide specific conditions for maintaining the ICM cells. Thomson is relied upon for the disclosure that purified preparations of primate and human embryonic stem cells can be isolated from the ICM of an embryo, and for providing specific conditions for maintaining primate and human ES cells in culture. Applicants arguments are not persuasive because Newman-Smith *et al.* provide the teaching and the necessary guidance for the practicing the method as claimed. Each of the limitations encompassed by the claim to produce parthenotes and obtain pluripotent embryonic stem cells from the resulting ICM cells are set forth by Newman-Smith *et al.* Thomson provides the necessary guidance to practice the methods taught by Newman-Smith *et al.* in mice to higher mammals such as primates and humans.

Thus, the claimed invention, as a whole was *prima facie* obvious absent to the evidence to the contrary.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers

must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800 1630